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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/051,311

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Jan-Michael Peters

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EXAMINER

FRONDA, CHRISTIAN L

ART UNIT

PAPER NUMBER

1652

DATE MAILED: 05/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No. 10/051,311	Applicant(s) PETERS ET AL	
	Examiner Christian L. Fronda	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 09 February 2006.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-6 and 11-16 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-5 and 11-15 is/are rejected.
- 7) ☒ Claim(s) 6 and 16 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 22 January 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

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### DETAILED ACTION

1. Claims 1-6 and 11-16 are pending and under consideration in this Office Action.

#### *Claim Rejections - 35 U.S.C. § 112, 1st Paragraph*

2. Claims 1-5 and 11-15 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for identifying a test compound that inhibits the proteolytic activity of a separase using a substrate peptide consisting of SEQ ID NO:9, SEQ ID NO: 11, or SEQ ID NO: 12; does not reasonably provide enablement for any method for identifying a test compound that inhibits the proteolytic activity of a separase using any substrate peptide comprising an amino acid sequence EXXR, wherein X is any amino acid. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Applicants' arguments filed 02/09/2006 have been acknowledged but are not persuasive. Applicants' position is that a *prima facie* case of lack of enablement has not been presented. Applicants argue that the cited references of Smith et al. and Cryns et al. supports applicants' assertion that making and identifying separase substrates would not have required undue experimentation. Applicants argue that no evidence or sound scientific reasoning has been presented to indicate that the screening methods taught by the specification would have involved a level of difficulty that would amount to undue experimentation. Applicants assert that the screening methods presented in the specification and available in the art as exemplified in the references of Smith et al. and Cryns et al. would have enabled a skilled person to easily and routinely identify EXXR-containing substrates including substrates with modified or non-naturally occurring amino acids. The examiner appreciates applicants' arguments but respectfully disagrees for reasons of record as supplemented below.

As stated in the previous Office Action, the nature and breadth of the claims encompass any method for identifying a test compound that inhibits the proteolytic activity of a separase using any substrate peptide comprising an amino acid sequence EXXR, wherein X is any amino acid. The examiner takes the position that these separase substrates containing EXXR encompass any peptide comprising any number of amino acid residues including modified and non-naturally occurring amino acid residues.

The specification does not provide any guidance or prediction on how the length or the composition of the of the peptide containing EXXR would affect the ability of the separase to

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recognize and hydrolyzes the peptide. The specification does not provide any indication where the EXXR should be in relation to the N- or C-terminal of the peptide which will enable the separase to recognize and hydrolyze the peptide. It is not clear from the specification if large peptides comprising EXXR would be hydrolyzed by separase since the specification discloses that small peptides consisting of SEQ ID NO:9, SEQ ID NO: 11, or SEQ ID NO: 12 were found to be separase substrates. While the cited references of Smith et al. and Cryns et al. describe general methods for searching and screening for protease substrates, the prior art does not provide guidance or prediction on whether any peptide comprising EXXR and any number of amino acid residues including modified and non-naturally occurring amino acid residues would be hydrolyzed by separase.

The examiner takes the position that trial and error experimentation used for searching and screening for specific peptides comprising EXXR, where such peptides are not limited by amino acid composition and number of residues, must be performed to ascertain which peptides are substrates for separase. In absence of any guidance and prediction from the specification and the art, this experimentation is undue and is outside the realm of routine experimentation. Thus, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with the claims.

Amending the claims to recite a substrate peptide consisting of SEQ ID NO:9, SEQ ID NO: 11, or SEQ ID NO: 12 may overcome the rejection.

3. Claims 1-5 and 11-15 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention

Applicants' arguments filed 02/09/2006 have been acknowledged but are not persuasive. Applicants' position that the expression "separase substrate comprising an amino acid sequence EXXR" do not refer to new or unknown biological materials that ordinary skilled artisans would easily miscomprehend, persons of skill in the art would understand that the substrates include the EXXR amino acid motif and are capable of being cleaved by an active separase, and that Example 18 of the USPTO's "Synopsis of Application of Written Description Guidelines" supports applicants' assertion that the claims meet the enablement requirement. The examiner appreciates applicants' arguments but respectfully disagrees for reasons of record as supplemented explained below.

As stated in the previous Office Action, the claims are genus claims that encompass a

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genus of peptides of any amino acid sequence, structure, and biological function comprising the amino acid sequence EXXR, where X is any amino acid, or comprising the amino acid sequence of SEQ ID NO: 9, SEQ ID NO: 11, and SEQ ID NO: 12. The genus of peptides containing EXXR, SEQ ID NO: 9, SEQ ID NO: 11, or SEQ ID NO: 12 encompass any peptide comprising any number of amino acid residues including modified and non-naturally occurring amino acid residues. The scope of the genus is not limited to peptides "consisting" of EXXR, SEQ ID NO: 9, 11, or 12 since the claims specifically recite the phrase "comprising an amino acid sequence".

The specification does not disclose how the length or the composition of the of the peptide containing EXXR would affect the ability of the separase to recognize and hydrolyzes the peptide. The specification does not disclose where the EXXR should be in relation to the N- or C-terminal of the peptide which will enable the separase to recognize and hydrolyze the peptide. It is not clear from the specification if large peptides comprising EXXR would be hydrolyzed by separase since the specification discloses that small peptides consisting of SEQ ID NO:9, SEQ ID NO: 11, or SEQ ID NO: 12 were found to be separase substrates. It is not clear from the specification that these small peptides consisting of SEQ ID NO:9, SEQ ID NO: 11, or SEQ ID NO: 12 is representative of the entire claimed genus of peptides having EXXR, where the claimed genus encompass any peptide comprising any number of amino acid residues including modified and non-naturally occurring amino acid residues. Thus, the skilled artisan cannot predict the structure of other peptides which are separase substrates as encompassed by the claimed genus

Thus, applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize applicants were in possession of the claimed genus of peptides of any amino acid sequence, structure, and biological function comprising the amino acid sequence EXXR, where X is any amino acid, or comprising the amino acid sequence of SEQ ID NO: 9, SEQ ID NO: 11, and SEQ ID NO: 12.

Example 18 of the USPTO's Synopsis of Application of Written Description Guidelines" is not directed toward an assay method using a genus of substrates comprising the amino acid sequence EXXR. Example 18 is only directed toward a method of expressing a protein of interest in *Neurospora crassa* mitochondria. Thus, applicants' argument that the claimed invention meets the written description requirement in view of Example 18 of the Patent Office's Written Description Guidelines is not accurate.

Amending the claims to recite a substrate peptide consisting of SEQ ID NO:9, SEQ ID NO: 11, or SEQ ID NO: 12 may overcome the rejection.

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*Conclusion*

4. No claim is allowed.

5. Claims 6 and 16 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.


6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christian L Fronda whose telephone number is (571)272-0929. The examiner can normally be reached Monday-Friday between 9:00AM - 5:00PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura N Achutamurthy can be reached on (571)272-0928. The fax phone number for the organization where this application or proceeding is assigned is (571)273-8300.

8. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CLF

  
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